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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,909	07/21/2003	Eileen Tozer	D1410-2US	7087

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EXAMINER
BERTAGNA, ANGELA MARIE

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
08/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/624,909	TOZER ET AL.	
	Examiner	Art Unit	
	ANGELA BERTAGNA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☒ Claim(s) *189* is/are allowed.

6)☒ Claim(s) *1,14,15,33,35,43-45,48,49,87,188,207,217,218 and 225-228* is/are rejected.

7)☒ Claim(s) *33,218 and 225* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,14,15,33,35,42-45,48,49,51,54,56,58,87,106,107,111,113,116,138,143,174,175,177,182,184,187-190,207,208 and 215-231.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 42,51,54,56,58,106,107,111,113,116,138,143,174,175,177,182,184,187,190,208,215,216,219-224 and 229-231.

DETAILED ACTION

Status of the Application

1. Applicant's response filed on May 20, 2009 is acknowledged. Claims 1, 14, 15, 33, 35, 42-45, 48, 49, 51, 54, 56, 58, 87, 106, 107, 111, 113, 116, 138, 143, 174, 175, 177, 182, 184, 187-190, 207, 208, and 215-231 are currently pending. In the response, Applicant amended claims 1, 33, 35, 87, 188, 189, 207, 218, and 225-227 and canceled claims 29 and 40. Claims 42, 51, 54, 56, 58, 106, 107, 111, 113, 116, 138, 143, 174, 175, 177, 182, 184, 187, 190, 208, 215, 216, 219-224, and 229-231 remain withdrawn from consideration as being drawn to a non-elected invention.

The following include new grounds of rejection necessitated by Applicant's amendments to the claims. Any previously made rejections or objections not reiterated below have been withdrawn as being obviated by the amendment. Applicant's arguments filed on May 20, 2009 that remain pertinent to the new grounds of rejection below have been fully considered, but they were not persuasive for the reasons set forth below. Accordingly, this Office Action is **FINAL**.

Election/Restrictions

2. This application contains claims 42, 51, 54, 56, 58, 106, 107, 111, 113, 116, 138, 143, 174, 175, 177, 182, 184, 187, 190, 208, 215, 216, 219-224, and 229-231 drawn to an invention nonelected with traverse in the reply filed on July 19, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Objections

3. Claim 33 is objected to because of the following informalities: Deleting the words "a sequence comprising" in line 3 is suggested to improve the readability of the claim. Also, replacing "the nucleic acid" in line 6 with "the nucleic acid encoding a fluorescent polypeptide" is suggested to improve consistency within the claim.

Claim 218 is objected to because of the following informalities: Inserting the word "of" after the phrase "step (c)" is suggested to improve the readability of the claim.

Claim 225 is objected to because of the following informalities: The recitation "deleting, or adding, or a combination thereof" is grammatically incorrect. Replacing this phrase with "deleting and/or adding and/or modifying" is suggested.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 1st paragraph (Written Description)

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 14, 15, 35, 43-45, 48, 49, 87, 188, 217, 218, and 225-228 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The central inquiry when considering written description is whether an ordinary artisan would reasonably conclude that Applicant was in possession of the claimed invention at the time of filing (see MPEP 2163 and *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1566-67, 43 USPQ2d 1398, 1404-05 (Fed. Cir. 1997); *Hyatt v. Boone*, 146 F.3d 1348, 1354, 47 USPQ2d 1128, 1132 (Fed. Cir. 1998)).

According to Revision I of the Written Description Training Materials (posted 4/11/08 at http://www.uspto.gov/web/menu/written/pdf), the following factors should be considered, when evaluating a claim for compliance with the written description requirement: (a) actual reduction to practice, (b) disclosure of drawings or structural chemical formulas (c) sufficient relevant identifying characteristics (d) method of making the claimed invention, (e) level of skill and knowledge in the art, and (f) predictability in the art (see page 1 of the Training Materials).

The instant claims are drawn to isolated nucleic acids that encode a fluorescent polypeptide and are at least 95%, 97%, or 98% identical to SEQ ID NO: 29 and compositions (*e.g.* vectors, host cells) comprising said nucleic acids. The genus of nucleic acids having at least 95%, 97%, or 98% identity to SEQ ID NO: 29 is very large and includes hundreds of thousands of structurally distinct molecules, each of which may encode a polypeptide having different

functional properties. The claims limit this large genus to nucleic acids that encode a fluorescent protein.

The specification teaches the nucleic acid sequence of SEQ ID NO: 29 (see page 17 of the Sequence Listing), and therefore, it contains an actual reduction to practice of one member within the claimed genus. The specification also discloses nucleic acids having at least 95% identity to SEQ ID NO: 29 (see, for example SEQ ID NO: 17). However, the specification does not disclose those regions of SEQ ID NO: 29 that are critical for conferring fluorescence activity to the encoded protein. There is a high degree of unpredictability in the art regarding structure-function correlations, and even a single nucleotide substitution can abolish the function of the protein encoded by a mutant nucleic acid. Accordingly, the level of skill in the art is high. The claimed nucleic acids do not show a significant level of similarity to other fluorescent proteins known in the art, and the specification does not teach that motifs known to be critical for fluorescence activity in these proteins are present in the proteins encoded by the claimed nucleic acids. As a result, the specification fails to adequately describe the relevant identifying characteristics that are critical for determining whether a giving nucleic acid having at least 95%, 97%, or 98% identity to SEQ ID NO: 29 also has the required functional property of fluorescence. In the absence of such disclosure, it must be concluded that Applicant was not in possession of the claimed invention at the time of filing.

Claim Rejections - 35 USC § 112, 1st paragraph (Enablement)

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

> pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 14, 15, 35, 43-45, 48, 49, 87, 188, 217, 218, and 225-228 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The Nature of the Invention & Breadth of the Claims

The instant claims are drawn to isolated nucleic acids that encode a fluorescent polypeptide and are at least 95%, 97% or 98% identical to SEQ ID NO: 29 and compositions (*e.g.* vectors, host cells) comprising said nucleic acids. The genus of nucleic acids having at least 95%, 97%, or 98% identity to SEQ ID NO: 29 is very large and includes hundreds of thousands of structurally distinct molecules, each of which may encode a polypeptide having different functional properties. The claims limit this large genus to nucleic acids that encode a fluorescent protein.

Guidance in the Specification and Working Examples

The specification teaches the nucleic acid sequence of SEQ ID NO: 29 (see page 17 of the Sequence Listing), and therefore, it contains an actual reduction to practice of one member within the claimed genus. The specification also discloses nucleic acids having at least 95% identity to SEQ ID NO: 29 (see, for example SEQ ID NO: 17). However, the specification does not disclose those regions of SEQ ID NO: 29 that are critical for conferring fluorescence activity to the encoded protein. There is no discussion in the specification of motifs or regions in SEQ ID NO: 29 that are critical for conferring this required functional property.

The working examples (see pages 155-159) also do not describe the regions of the disclosed nucleic acids that are critical for encoding a functional (*i.e.* fluorescent) protein. In Example 1 cDNA libraries prepared from marine sources were analyzed to identify cDNA clones encoding fluorescent proteins (see pages 155-156). In Example 2 (see pages 156-158), fluorescent proteins were isolated and purified. In Example 3 (see pages 158-159), the excitation and emission properties for a subset of the disclosed fluroescent proteins was determined. However, Examples 1-3 do not provide any discussion of regions of the proteins that are required for fluorescence activity.

State of the Prior Art and Unpredictability

The prior art does not teach isolated nucleic acids that are at least 95% identical to SEQ ID NO: 29 and encode a fluorescent polypeptide. The claimed nucleic acids do not show a significant level of similarity to other fluorescent proteins known in the art, and therefore, the art does not identify regions or motifs in the claimed nucleic acids that are critical for fluorescence

activity. There is a high degree of unpredictability in the art regarding structure-function correlations, and it is well established that even a single nucleotide substitution can abolish the function of the protein encoded by the mutant nucleic acid. Therefore, it is highly unpredictable whether or not a given nucleic acid having at least 95% identity to SEQ ID NO: 29 will have fluorescence activity, especially since neither the specification nor the art teaches the regions of the protein that are critical for maintaining fluorescence activity.

Quantity of Experimentation

The quantity of experimentation required in this case is immense, because it would require significant study and experimentation to determine whether a nucleic acid having at least 95% identity to SEQ ID NO: 29 also encodes a fluorescent protein. Each different variant nucleic acid would have to be produced via mutagenesis, and the encoded proteins would have to be expressed and characterized functionally. In the absence of any guidance in the specification or the art regarding regions of SEQ ID NO: 29 that are critical for determining fluorescence activity, the ordinary artisan would have little or no starting point for determining whether a given variant of SEQ ID NO: 29 encodes a fluorescent protein. Given the unpredictability in the art regarding the effect of nucleic acid mutations on the functionality of the proteins encoded therefrom, the ordinary artisan would be required to undertake this large quantity of experimentation with little or no guarantee of success.

The Level of skill in the art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, the instant claims are broadly drawn to isolated nucleic acids having at least 95% identity to SEQ ID NO: 29 and that encode a fluorescent protein. Despite the breadth of the claims, the specification only teaches a small number of nucleic acids falling within the claimed genus and provides no guidance regarding the regions of SEQ ID NO: 29 that are required for the fluorescence activity of the claimed proteins. Thus, given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to determine those regions of SEQ ID NO: 29 required for fluorescence activity, the lack of guidance provided in the specification, balanced only against the high skill level in the art, it is the position of the examiner that the claimed nucleic acid products fail to comply with the enablement requirement.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 33 is rejected under 35 U.S.C. 102(b) as being anticipated by Adams (Molecular and Cellular Endocrinology (1995) 108: 23-33; newly cited).

Regarding claim 33, Adams teaches random decamers (page 24, column 2). The random decamers taught by Adams inherently include a sequence having ten consecutive nucleotides of a

nucleic acid of claim 1 or a complement thereof. Therefore, the random decamers of Adams anticipate the nucleic acid probe of claim 33.

Allowable Subject Matter

7. Claim 189 is allowed.

Response to Arguments

8. Applicant's arguments filed on May 20, 2009 remain pertinent to the rejections made above under 35 U.S.C. 112, first paragraph (enablement and written description). These arguments have been fully considered, but they were not persuasive. Applicant argues that the rejections have been obviated by the claim amendments (see page 16). This argument was not persuasive, because as discussed in greater detail above, the amended claims do not satisfy the enablement and written description requirements of 35 U.S.C. 112, first paragraph. Since Applicant's arguments were not persuasive, the rejections have been maintained with modification as necessary to account for the claim amendments.

Applicant's remaining arguments filed on May 20, 2009 have been considered, but they are moot since they are directed to objections and rejections that have been withdrawn in view of the amendment.

Conclusion

9. No claims are currently allowable. Claims 1, 14, 15, 35, 43-45, 48, 49, 87, 188, 217, 218, and 225-228 are free of the art, but they have been rejected for failing to comply with the requirements of 35 U.S.C. 112, first paragraph.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 9- 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

amb

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637